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Dated: November 15, 2002

Signature: 

(Brent LaBerge)

Docket No.: HMSU-P11-006
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ingham et al.

Application No.: 08/954771

Group Art Unit: 1646

Filed: October 20, 1997

Examiner: M. Brannock

For: VERTEBRATE EMBRYONIC PATTERN-
INDUCING PROTEINS AND USES RELATED
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Commissioner for Patents
Washington, DC 20231

Dear Sir:

Submitted herewith is one set (nineteen sheets, sixteen figures) of formal drawings for filing in the above-identified patent application. Kindly substitute the enclosed formal drawings for the informal drawings submitted with the originally filed application.

Applicants believe no fee is due other than the fees for filing a CPA. However, if an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. HMSU-P11-006 from which the undersigned is authorized to draw.

Dated: November 15, 2002

Respectfully submitted,

By 

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A.g.
12/4/02



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RCKEKLNVLAYSVMNEWPGIRLLVT
RCKERVNSLAIAVMHMWPGVRLRVT
RCKDKLNALAISVMNQWPGVKLLRVT

DROSOPHILA HEDGEHOG
CHICKEN HEDGEHOG-A
CHICKEN HEDGEHOG-B

ESWDEDYHHGQESLHYEGRAVTIAT
EGWDEDEGHHLPDSLHYEGRALDITTT
EGWDEDEGHHSEESLHYEGRAVDITTT

DROSOPHILA HEDGEHOG
CHICKEN HEDGEHOG-A
CHICKEN HEDGEHOG-B

SDRDQSKYGMRLARLAVEAGFDWV
SDRDRHKYGMRLARLAVEAGFDWV
SDRDRSKYGMRLARLAVEAGFDWV

DROSOPHILA HEDGEHOG
CHICKEN HEDGEHOG-A
CHICKEN HEDGEHOG-B

Fig. 1



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1	-----	CHICKEN SONIC HEDGEHOG
1	MDNHSSVPWASAAASVTCLSLDAKCHSSSSSSSSSKSAASSI	DROSOPHILA HEDGEHOG
1	-----MVEMILLTRILLVGFICALLVS	CHICKEN SONIC HEDGEHOG
41	SAIPQEETQTMRIAHTQRCLSRLTSLVALLLIVLPMVFS	DROSOPHILA HEDGEHOG
23	SGLTCGPGRGIGKRRHPKLTPLAYKQFIPNVAEKTLGAS	CHICKEN SONIC HEDGEHOG
81	PAHSCGPGRGLGRHR-ARNLYPLVLKOTIPNLSEYTNAS	DROSOPHILA HEDGEHOG
63	GRYEGKITRNSERFKELTPNYNPDIIIFKDEENTGADRLMT	CHICKEN SONIC HEDGEHOG
120	GPLEGVIRRDSPKFKDLVPNYNRDILFRDEEGTGADRLMS	DROSOPHILA HEDGEHOG
103	QRCKDKLNALATSVMNQWPGVKLRVTEGWDEDGHHSEESI	CHICKEN SONIC HEDGEHOG
160	KRCCKEKLNVLANSVMNEWPGIRLLVTESWDEDVHHGOESI	DROSOPHILA HEDGEHOG
143	HYEGRVDTITSDRDRSKYGMLARLAVEAGFDWVYYESKA	CHICKEN SONIC HEDGEHOG
200	HYEGRVTLATSDRDQSKYGMLARLAVEAGFDWVSYSRR	DROSOPHILA HEDGEHOG
183	HIHCSVKAENSVAAKSGGCFPGSATVHLEHGGTKLVKDLIS	CHICKEN SONIC HEDGEHOG
240	HIYCSVKSDSSISSHVHGCFTPESTALLESGVRKPLGELS	DROSOPHILA HEDGEHOG
223	PGDRVLAADADGRLLYSDFLTFLDRMDSSRKLFYVIETRO	CHICKEN SONIC HEDGEHOG
280	IGDRVLSMTANGQAVYSEVILEMDRNLEQMONEVOLHT-D	DROSOPHILA HEDGEHOG
263	PRARILLTAAHLLFVAPQHNQSEATGSTSGQALFASNVPK	CHICKEN SONIC HEDGEHOG
319	GGAVLTVTIPAHLVSVWQ-----PESQKLTFVFADRIEE	DROSOPHILA HEDGEHOG
303	GQRVYVLGEGGQQLLPASVHSVSLREEASGAYAPLTAQGT	CHICKEN SONIC HEDGEHOG
352	KNOVLVRDVETGELRFPQRVVKVG-SVRSKGVVAPLTRECT	DROSOPHILA HEDGEHOG
343	ILLNRVLASCYAVIEEHSWAHWAFAPFRLAQGL---LAA-	CHICKEN SONIC HEDGEHOG
391	IVVNSVAASCYAVINSQSLAHWGLAPMRLSTLEAWLPAK	DROSOPHILA HEDGEHOG
379	--LCPDGAIPTAATTTTGIHWYSRLLYRIGSWVLDGDALH	CHICKEN SONIC HEDGEHOG
431	EQLHSSPKVVSSAQOQNGIHWYANALYKVKDYVLPQSWRH	DROSOPHILA HEDGEHOG
417	PLGMVAPAS	CHICKEN SONIC HEDGEHOG
471	D	DROSOPHILA HEDGEHOG

Fig. 2



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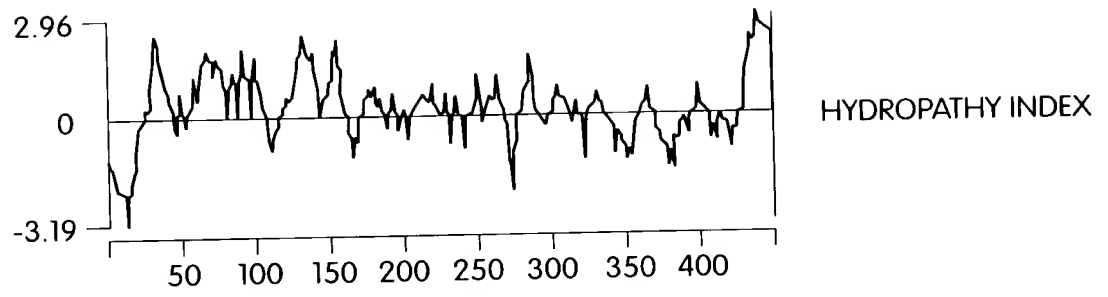


Fig. 3



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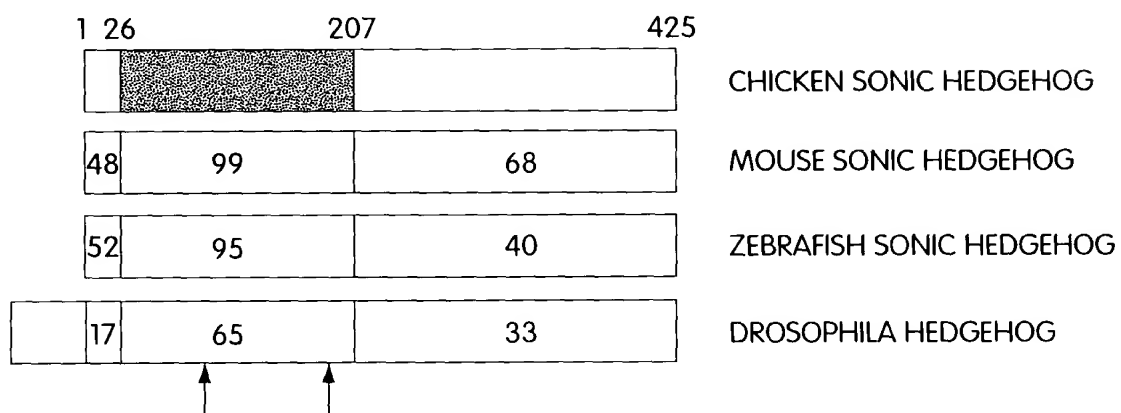


Fig. 4



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D-hh	¹ MDNHSSVPWA	SAASVTCLSL	DAKCHSSSSS	SSSKSAASSI	SAIPQEETQT
M-Dhh
M-Ihh
M-Shh
C-Shh
Z-Shh
D-hh	⁵¹ MRHIAHTQRC	LSRLTSLVAL	LLIVLPMVFS	^Y PAHSCGPGRG	LGRHR...AR
M-DhhMALPASLL	PLCCLALLAL	SAQSCGPGRG	PVGRRRYVRK
M-Ihh
M-Shh	MLLLLARCFL	VILASSLLVC	PGLACGPGRG	FGKRRH..PK
C-ShhMV	EMLLLTRILL	VGFICALLVS	SGLTCGPGRG	IGKRRH..PK
Z-ShhMRLLTRVLL	VSLTSLV	SGLACGPGRG	YGRRRH..PK
D-hh	¹⁰¹ NLYPLVLKQT	IPNLSEYTNS	ASGPLEGVIR	RDSPKFKDLV	PNYNRDILFR
M-Dhh	QLVPLLYKQF	VPSMPERTLG	ASGPAEGRVT	RGSERFRDLV	PNYNPDIIFFK
M-IhhERFKELT	PNYNPDIIFFK
M-Shh	KLTPLAYKQF	IPNVAEKTG	ASGRYEGKIT	RNSERFKELT	PNYNPDIIFFK
C-Shh	KLTPLAYKQF	IPNVAEKTG	ASGRYEGKIT	RNSERFKELT	PNYNPDIIFFK
Z-Shh	KLTPLAYKQF	IPNVAEKTG	ASGRYEGKIT	RNSERFKELT	PNYNPDIIFFK
D-hh	¹⁵¹ DEEGTGADRL	^Y MSKRCKEKLN	VLAYSVMNEW	PGIRLLVTES	WDEDYHHGQE
M-Dhh	DEENSGADRL	MTERCKERVN	ALAIAMNMW	PGVRLRVTEG	WDEGDHHAQD
M-Ihh	DEENTGADRL	MTQRCKDRLN	SLAISVMNQW	PGVKLRVTEG	RDEGDHHSSE
M-Shh	DEENTGADRL	MTQRCKDKLN	ALAISVMNQW	PGVRLRVTEG	WDEGDHHSSE
C-Shh	DEENTGADRL	MTQRCKDKLN	ALAISVMNQW	PGVKLRVTEG	WDEGDHHSSE
Z-Shh	DEENTGADRL	MTQRCKDKLN	SLAISVMNHW	PGVKLRVTEG	WDEGDHHSFE
D-hh	²⁰¹ SLHYEGRVAVT	IATSDRDQSK	YGMLARLAVE	AGFDWVSYSVS	RRHIYCSVKS
M-Dhh	SLHYEGRALD	ITTSDRDRNK	YGLLARLAVE	AGFDWVYYES	RNHIHVSVKA
M-Ihh	SLHYEGRVAVD	ITTSDRDRNK	YGLLARLAVE	AGFDWVYYES	KAHVHCSVKS
M-Shh	SLHYEGRVAVD	ITTSDRDRSK	YGMLARLAVE	AGFDWVYYES	KAHIHCSVKA
C-Shh	SLHYEGRVAVD	ITTSDRDRSK	YGMLARLAVE	AGFDWVYYES	KAHIHCSVKA
Z-Shh	SLHYEGRVAVD	ITTSDRDKSK	YGTLSRLAVE	AGFDWVYYES	KAHIHCSVKA
D-hh	²⁵¹ DSSISSHVHG	CFTPESTALL	ESGVRKPLGE	LSIGDRVLMS	TANGQAVYSE
M-Dhh	DNSLAVRAGG	CFFGNATVRL	RSGERKGLRE	LHRGDWVLAA	DAAGRVVPTP
M-Ihh	EHSAAAKTGG	CFFPAGQVRL	ENGervalSA	VKPGDRVLAM	GEDGTPTFSD
M-Shh	ENSVAAKSGG	CFFPGSATVHL	EQGGTKLVKD	LRPGDRVLAA	DDQGRLLYSD
C-Shh	ENSVAAKSGG	CFFPGSATVHL	EHGGTKLVKD	LSPGDRVLAA	DADGRLLYSD
Z-Shh	ENSVAAKSGG	CFFGSALVSL	QDGGQKAVKD	LNPGDKVLAA	DSAGNLVFS
D-hh	³⁰¹ VILFMDRNLE	QMqNFVQLHT	.DGGAVLTVT	PAHLVSVWQ.PESQ
M-Dhh	VLLFLDRDLQ	RRASFVAVET	ERPPRKLTLT	PWHLVFAAR.	...GPAPAPG
M-Ihh	VLIFLDREPN	RLRAFQVIET	QDPPRLALT	PAHLLEFIADN	HTE...PAA
M-Shh	FLTFLDRDEG	AKKVFIYVIET	LEPRERLLLT	AAHLLFVAP.	HNDSGPTPGP
C-Shh	FLTFLDRMDS	SRKLFYVIET	RQPRARLLLT	AAHLLFVAPQ	HNQSEATGST
Z-Shh	FIMFTDRDST	TRRVFIYVIET	QEPVEKITLT	AAHLLFVLN	STEDLHTMT.

Fig. 5A-1



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	351				
D-hh	KLTFVFADRI	EEKNQVLV..	RDVETGELRP	QRVVKVG.SV	RSKGVVAPLT
M-Dhh	DFAPVFARRL	RAGDSVLA..	..PGGDALQP	ARVARVA.RE	EAVGVFAPLT
M-Ihh	HFRATFASHV	QPGQYVLV..	..SGVPGLQP	ARVAVS.TH	VALGSYAPLT
M-Shh	S..ALFASRV	RPGQRVYVVA	ERGGDRRLLP	AAVHSVTLRE	EEAGAYAPLT
C-Shh	SGQALFASNV	KPGQRVYVLG	E..GGQQLLP	ASVHSVSLRE	EASGAYAPLT
Z-Shh	...AAYASSV	RAGQKVMVVD	DSGQLKSVIV	QRIYT....E	EQRGSFAPVT
	401				
D-hh	REGTIVNSV	AASCYAVINS	QSLAHWGLAP	MRLSTLEAW	LPAKEQLHSS
M-Dhh	AHGTLLVNDV	LASCYAVLES	HQWAHRAFAP	LRLHALGAL	LP.....
M-Ihh	RHGTLVVEDV	VASCFAAVAD	HHLAQLAFWP	LRLFPSL...
M-Shh	AHGTILINRV	LASCYAVIEE	HSWAHRAFAP	FRLAHALLAA	LAPARTDGGG
C-Shh	AQGTILINRV	LASCYAVIEE	HSWAHWAFAP	FRLAQGLLAA	LCP.....
Z-Shh	AHGTIVVDRI	LASCYAVIED	QGLAHLAFAP	ARLYYYVSSF	LSP.....
	451				
D-hh	PKVV.....	...SSAQQQN	GIHWYANALY	KVKDYVLPQS	WRHD*
M-DhhGGAVQPT	GMHWYSRLLY	RLAEELMG*	
M-IhhAWGSWTPSE	GVHSYPQMLY	RLGRLLLEES	TFHPLGMSG
M-Shh	GGSIPAAQSA	TEARGAEPTA	GIHWYSQLLY	HIGTWLLDSE	RMHPLGMAVK
C-Shh	DGAIPTA...ATTTT	GIHWYSRLLY	RIGSWVLDGD	ALHPLGMVAP
Z-Shh	KTPAVGPMRL	YNRRGSTGTP	GSC.....H	QMGTWLLDSN	MLHPLGMSVN
	501				
M-Ihh	GS*				
M-Shh	SS*				
C-Shh	AS*				
Z-Shh	SS*				

Fig. 5A-2



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M-Dhh: CGPGRGPVGRRRYVVRKQLVPLLYKQFVPSMPERTLGASGPAEGRVTRGSSERFRDLV
M-Ihh: *****
H-Ihh: *****
H-Shh: CGPGRGFGKRRH**PKKLTPLAYKQFIPNVAEKTLGASGRYECKISRNSERFFKELT
C-Shh: CGPGRGIGKRRH**PKKLTPLAYKQFIPNVAEKTLGASGRYECKITRNSERFFKELT
M-Shh: CGPGRGFGKRRH**PKKLTPLAYKQFIPNVAEKTLGASGRYECKITRNSERFFKELT
Z-Shh: CGPGRGYGRRRH**PKKLTPLAYKQFIPNVAEKTLGASGRYECKITRNSERFFKELT
CON: CGPGRGXXXXRRXXPKKXLPLXYKQFXPXXEXTLGASGXEGXXRXSERFXXLT

PNYNPDIIFKDEENSGADRLMTERCCKERVNALAIAMNMWPGVRLRVTEGWDEDGH
PNYNPDIIFKDEENTGADRLMTQRCCKDRNLNSLAISVMNQWPGVKLRVTEGWDEDGH
*****RRRLMTQRCCKDRNLNSLAISVMNQWPGVKLRVTEGWDEDGH
PNYNPDIIFKDEENTGADRLMTQRCCKDKLNALAIISVMNQWPGVKLRVTEGWDEDGH
PNYNPDIIFKDEENTGADRLMTQRCCKDKLNALAIISVMNQWPGVKLRVTEGWDEDGH
PNYNPDIIFKDEENTGADRLMTQRCCKDKLNALAIISVMNQWPGVKLRVTEGWDEDGH
PNYNPDIIFKDEENTGADRLMTQRCCKDKLNALAIISVMNHWPVKLRVTEGWDEDGH
PNYNPDIIFKDEENXGADRLMTXRCCKXXXNLALAIISVMNXWPVKLRVTEGXDEDGH

HAQDSLHYEGRALDITTSDRDRNKYGLLARLAVEAGFDWVYYESRNIHVSVKAD
HSEESLHYEGRAVDITTSDRDRNKYGLLARLAVEAGFDWVYYESKAHVHCSVKSE
HSEESLHYEGRAVDITTSDRDRNKYGLLARLAVEAGFDWVYYESKAHVHCSVKSE
HSEESLHYEGRAVDITTSDRDRSKYGMRLARLAVEAGFDWVYYESKAHIHCSVKA
HSEESLHYEGRAVDITTSDRDRSKYGMRLARLAVEAGFDWVYYESKAHIHCSVKA
HSEESLHYEGRAVDITTSDRDRSKYGMRLARLAVEAGFDWVYYESKAHIHCSVKA
HFEESLHYEGRAVDITTSDRDRSKYGTLSRLAVEAGFDWVYYESKAHIHCSVKA
HXXXSLHYEGRAXDITTSDRDRXXXKYGXLRLAVEAGFDWVYYESXXXXHXXSVKXX

Fig. 5B



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	M-Dhh	M-lhh	C-Shh	Zf-Shh	D-hh
M-Shh	61 (77)	63 (78)	84 (92)	68 (80)	48 (64)
M-Dhh		58 (75)	61 (77)	54 (71)	51 (68)
M-lhh			64 (78)	61 (75)	48 (68)
C-Shh				68 (80)	49 (64)
Zf-Shh					47 (64)

Fig. 6

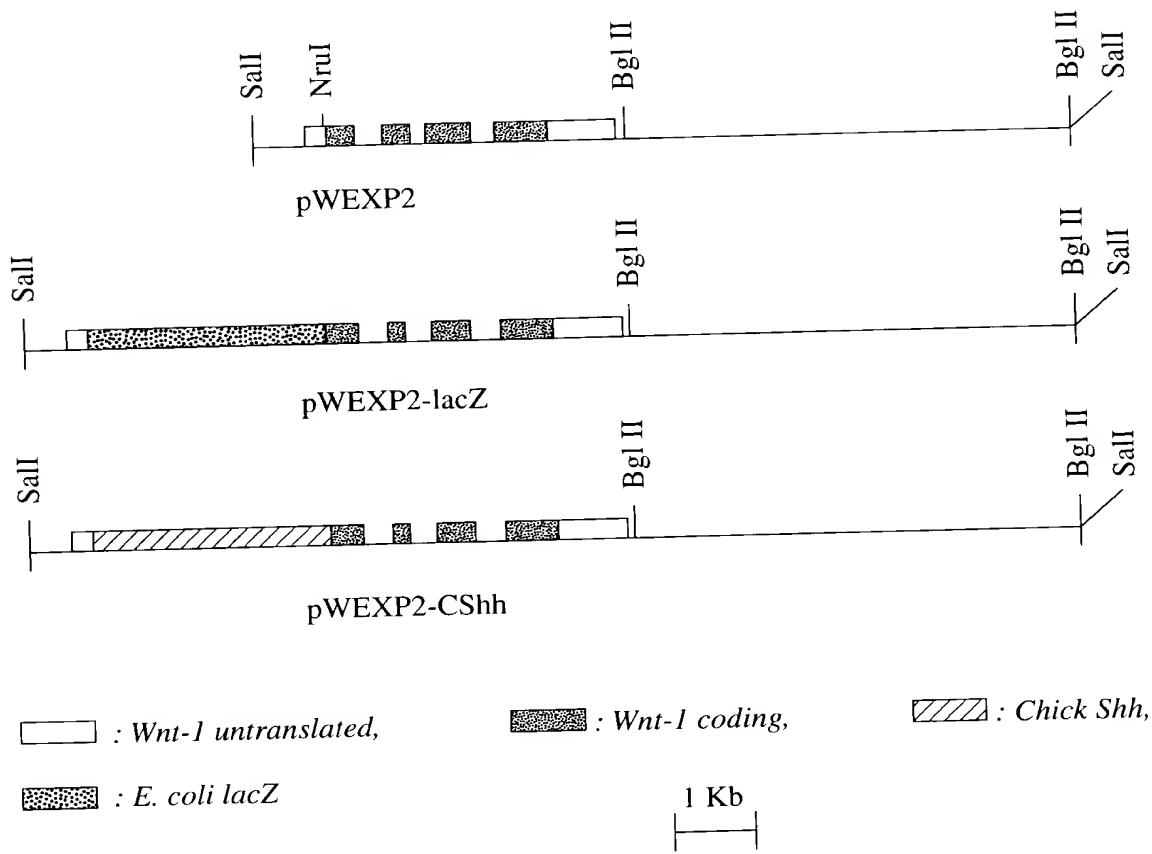
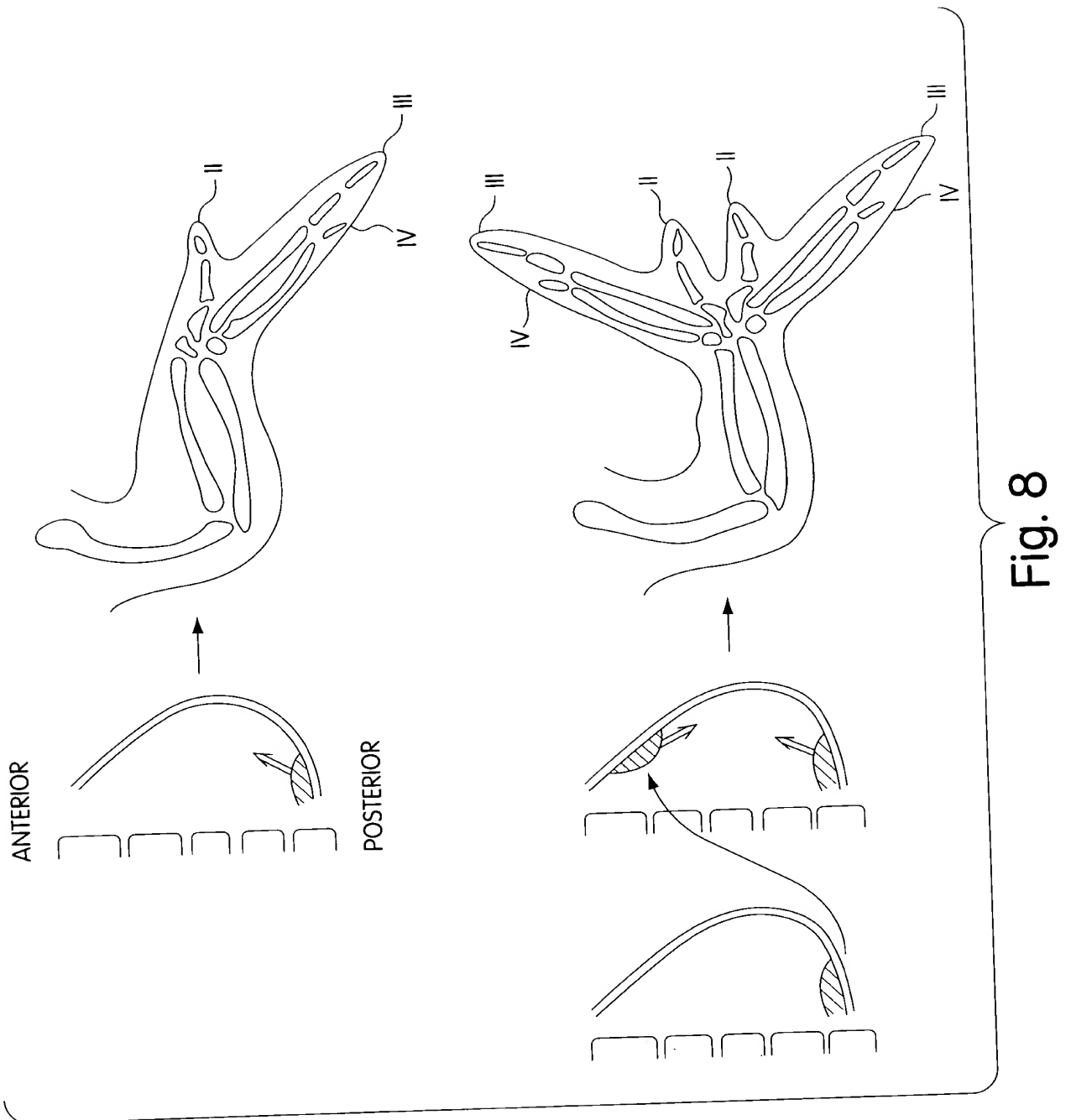
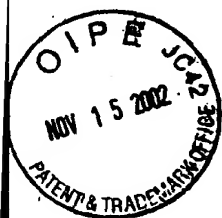


Fig. 7





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hh 1 MDNHSSVPWASAASVTCLSLDAKCHSSSSSSSSSSKSAASSISAIPQEETQT
shh
hh 51 MRHIAHTQRCLSR^YLTSLVALLLIVLPMVFSPAHS^YCGPGRGLGRHR.ARN^YL
shh 1MRL^YLTRVLLVSL^YLTSLVVS.GLACGPGRGYGRRRH^YPKKL
hh 100 YPLVLKQTIPNLSEYTNSASGPLEGVIRRDSPKF^YKDLVPN^YNRDILFRDE
shh 40 TPLAYKQFIPNVAEKT^YLGASGRYEGKITR^YNSERFKELTPN^YNPDIIFKDE
hh 150 EGTGADRLMSKRCKEKLNV^YLAYSVMNEWPGIRLVV^YTESWDEDYHHGQESL
shh 90 ENTGADRLMTQ^YRCKDKLNSLAISVMNHWPGVKLRV^YTEGWDEDGHHFEESL
hh 200 HYEGR^YAVTIATSDRDQSKYGMLARLAVEAGFDWVS^YYVSR^YRHIYCSVKSDS
shh 140 HYEGR^YAVDITTS^YDRDKSKYGTLSRLAVEAGFDWV^YYESKAHIHCSVKAEN
hh 250 SISSHVHGCF^YTPESTALLES^YGVRKPLGELS^YIGDRVLSMTANGQAVYSEVI
shh 190 SVAAKSGGCFPGSALVSLQDGGQKAVKDLNPGDKVLAADSAGNLVFSDFI
hh 300 LFMDRNLEQM^YQNFVQLHT.DGGAVLTVTPAHLVSVWQ^YPESQKL...TFVF
shh 240 MFTDRDSTTRRVFYVIETQEPVEKITLTA^YAHLLFVL^YDNSTEDLHTMTAAY
hh 347 ADRIEKNQVLVRDVETGELRPQ^YRVVKVGSVRSKGVVAPLTREGTIVVNS
shh 290 ASSVRAGQKVMVVD.DSGQLKSVIVQRIYTEEQRGSFAPVTAHGTIVVDR
hh 397 VAASCYAVINSQSLAHWGLAPMRL^YLLSTLEAWLPAKEQL.....HSS
shh 339 ILASCYAVIEDQGLAHLAFAPARLYYVSSFLSPKTPAVGPMRLYNRRGS
hh 438 PKV^YVSSAQQQNGIH^YWYANALYKVKDYVLPQSWRHD 471
shh 389 TGTPGSCHQMGTWLLDSNMLHPLGMSV..... 415

Fig. 9A

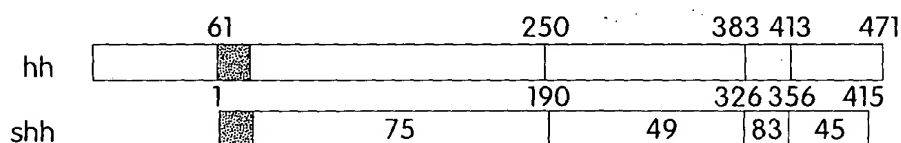


Fig. 9B



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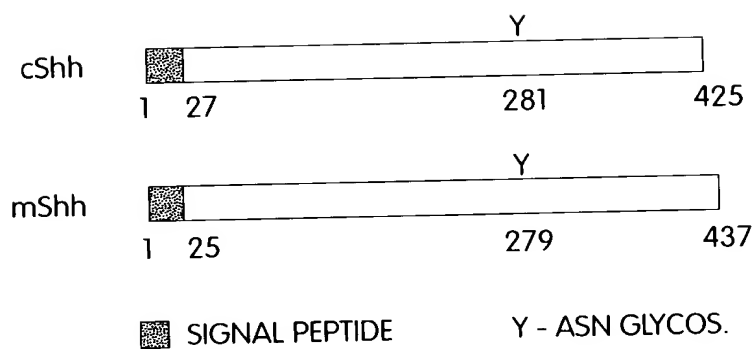


Fig. 11

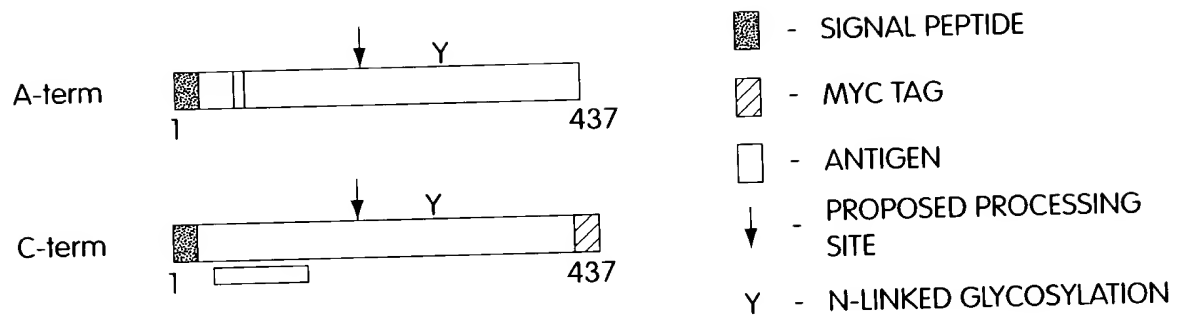


Fig. 12

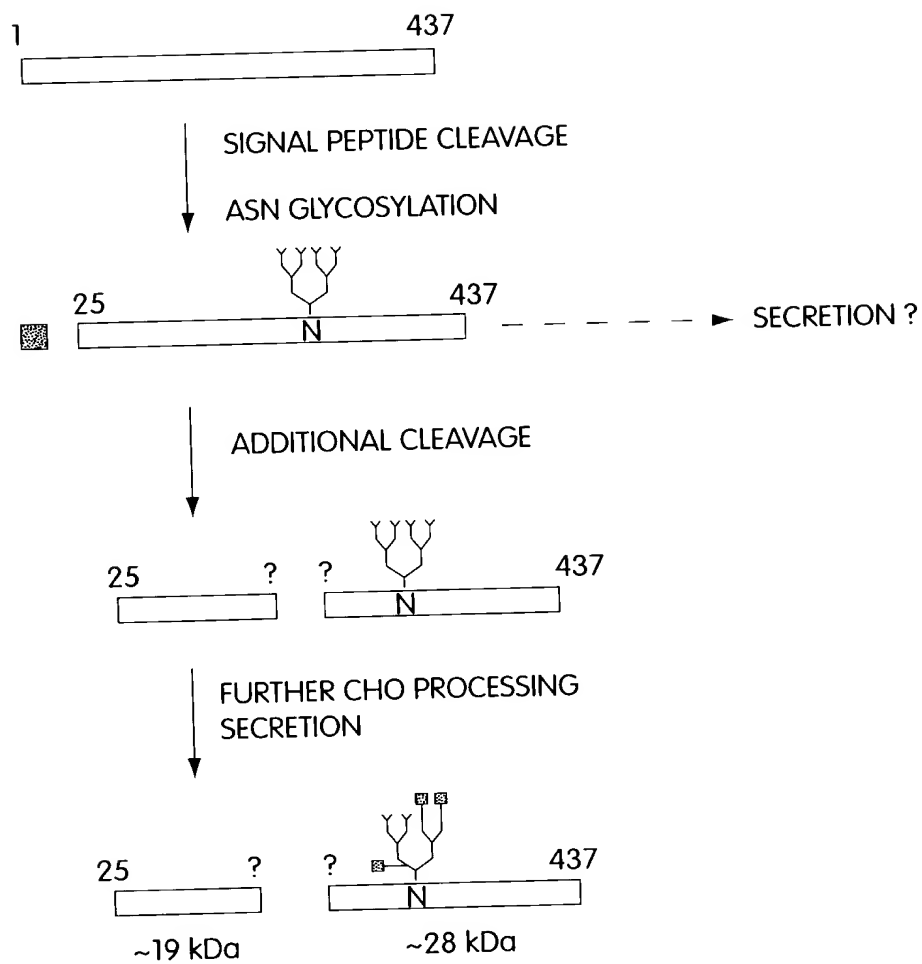


Fig. 13

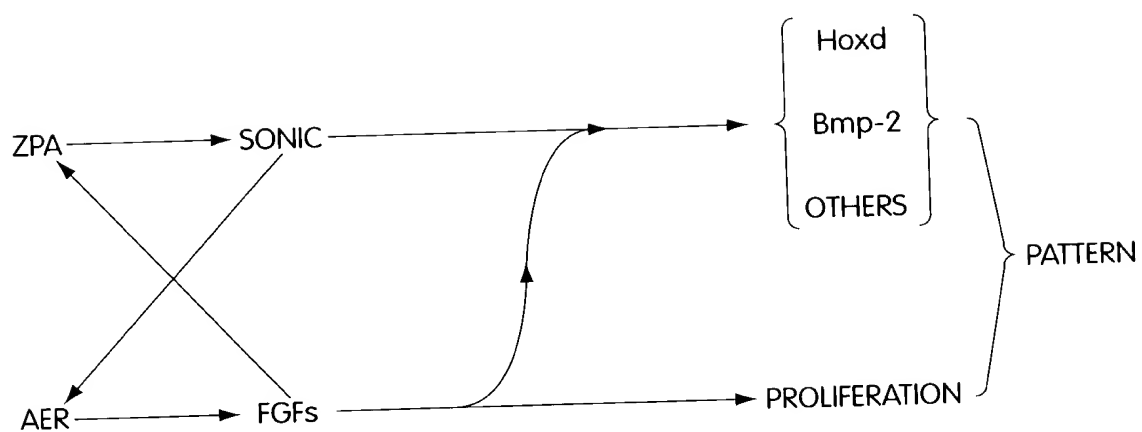


Fig. 14

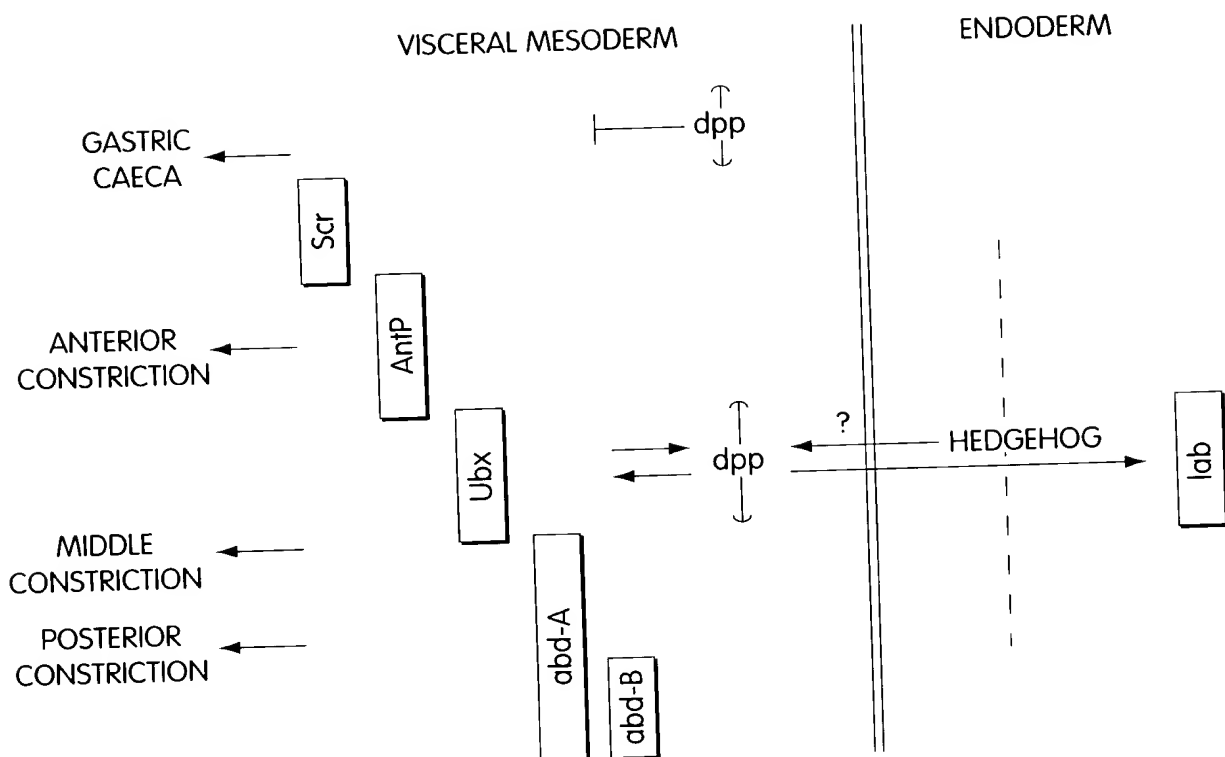


Fig. 15A

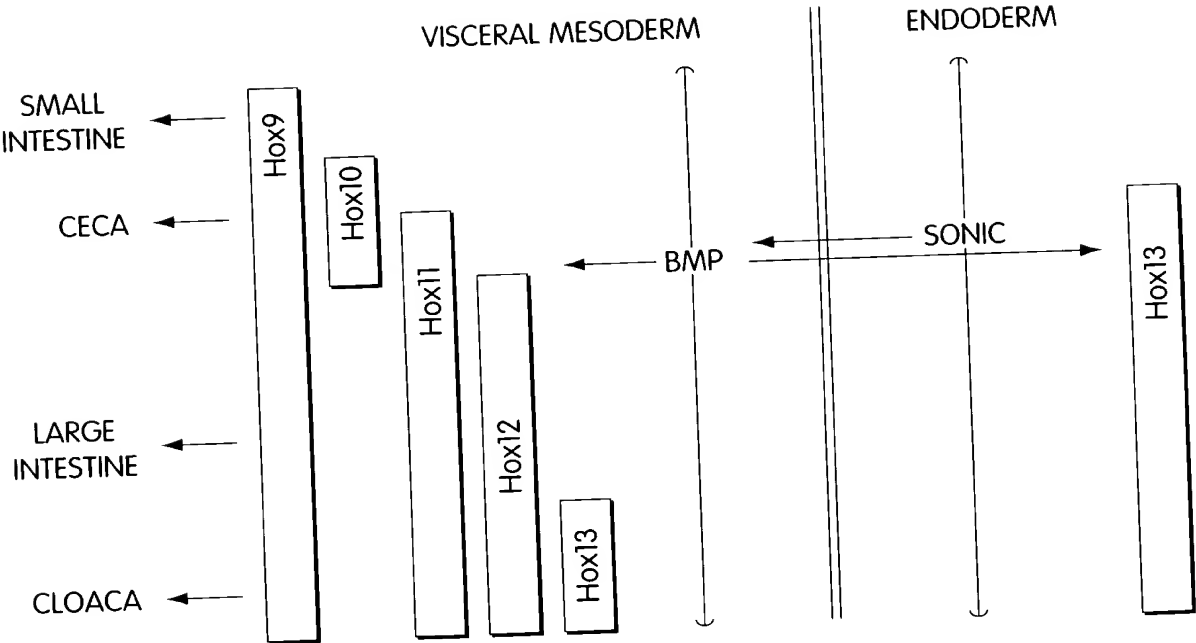


Fig. 15B

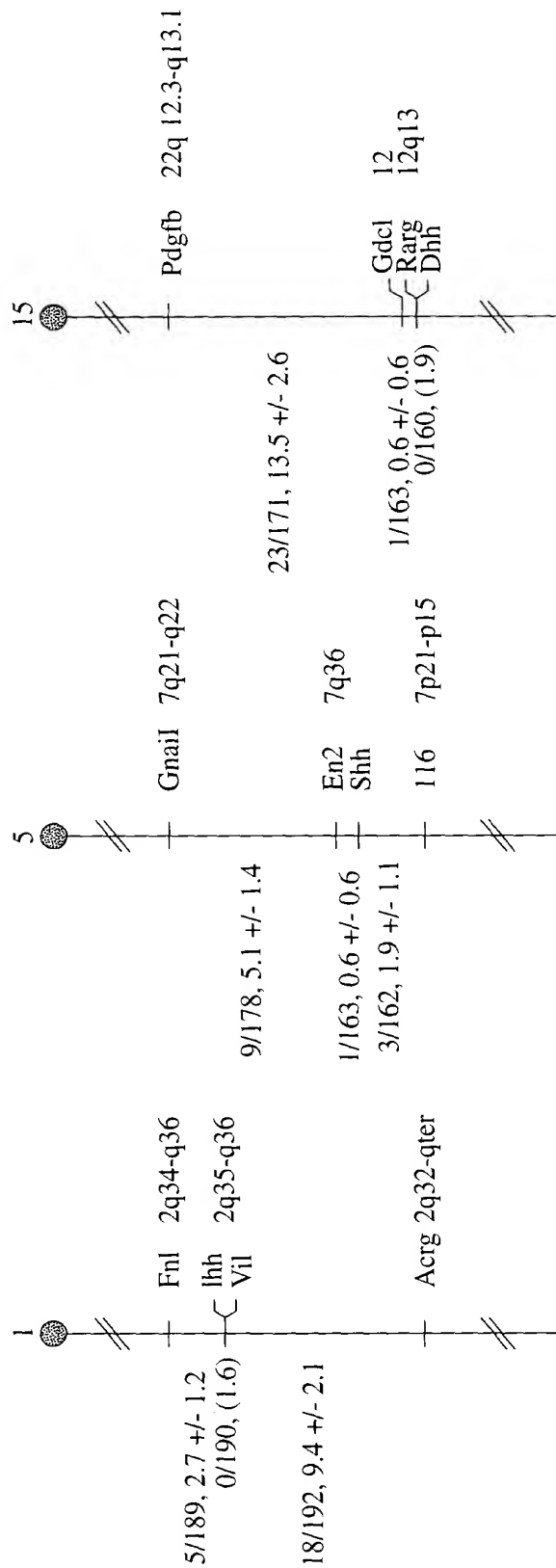
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Fig. 16